

Notice of Allowability	Application No.	Applicant(s)	
	09/593,914	HYLDIG-NIELSEN ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 10/28/2005.
2. ☒ The allowed claim(s) is/are 46-49,61,62,83-85 and 88-98.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|---|
| <ol style="list-style-type: none"> 1. <input type="checkbox"/> Notice of References Cited (PTO-892) 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | <ol style="list-style-type: none"> 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date <u>11/7/05</u>. 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance 9. <input type="checkbox"/> Other _____. |
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EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Brian Gildea on November 7, 2005.

The application has been amended as follows:

In claim 46, line 6, after "detecting enzyme activity", -- of the enzyme-linked probe or probes -- has been inserted.

In claim 83, line 11, after "detecting enzyme activity", -- of the enzyme-linked probe or probes -- has been inserted.

The title has been amended to read:

-- METHODS FOR THE DETECTION, IDENTIFICATION, AND/OR ENUMERATION OF YEAST, PARTICULARLY IN WINE --

THE FOLLOWING IS AN EXAMINER'S STATEMENT OF REASONS FOR ALLOWANCE:

The closest prior art of Schut (WO 99/10533) discusses methods of in situ hybridization to detect the presence of a microorganism wherein the methods comprise treating a microorganism with a solution to partly degrade the cell wall or membrane to thereby allow for penetration through the cell wall or membrane of an enzyme labeled probe (see abstract, claim 1, and pages 6-7). Schut teaches that probes labeled with

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horseradish peroxidase are too large to freely enter bacterial cells and therefore methods are needed to permeabilize the cell wall (page 16). Schut (page 4) notes that permeabilization of cells "gets more difficult for larger molecules since the margin between the accessibility of the target molecules and loss of target molecules or complete cell lysis becomes very narrow." To overcome these obstacles, Schut discloses specific conditions and reagents that can be used to permeabilize bacteria (see Table 8 and Example 9). Schut generally states that methods of in situ hybridization using labeled probes, such as enzyme-labeled probes, can be applied to any microorganism, including viruses, plasmids, yeasts, fungi, algae, and protozoa (see Abstract and claims 1, 2 and 12). However, Schut does not exemplify methods in which in situ hybridization with an enzyme-linked probe is used to detect yeast. Further, while Schut emphasizes the unpredictability of using enzyme-linked probes for in situ hybridization in microorganisms, Schut does not teach does not teach any permeabilization conditions that can be used in yeasts and does not provide sufficient guidance to enable the application of this technique to yeasts. The teachings of Amann also indicate the unpredictability of applying in situ hybridization with enzyme-linked probes to yeasts. Amann (page 3010) teaches that "Since even in an actively growing pure culture only some cells were stained, enzyme-labeled oligonucleotides cannot currently be used for specific single-cell identification of gram-positive bacteria. We encountered similar problems with cells of *Saccharomyces cerevisiae*, and again attempts to make the intracellular RNA accessible by enzymatic pretreatment (lyticase and β -glucuronidase; both from Sigma) of the cells or detergent failed. ... For now,

enzyme-labeled oligonucleotides can therefore be used only for specific identification and identification of gram-negative bacteria and several members of the *Euryarchaeota*." Amann (page 3010) also states that "Although we are optimistic that methods can be tailored for single strains under investigation, we do not expect to find a universal method that will permeablize the whole array of different microorganisms to comparable degrees." Accordingly, Amann does not provide sufficient guidance to enable a method for detecting yeasts by in situ hybridization using an enzyme-linked hybridization probe.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (571) 272-0747. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571)-272-0745.

The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866)-217-9197 (toll-free).

Carla Myers
November 7, 2005


CARLA J. MYERS
PRIMARY EXAMINER